DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/11 has been entered.

Status of Claims

2. Claims 1-10, 12, and 13 are pending in this application. Claim 11 stands canceled.

3. Claims 1-10, 12, and 13 are examined.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-10, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kita et al (US Patent 6,307,052, previously cited) in view of Lehmussaari et al (US Patent 5,795,913).

The claimed invention, as amended, is drawn to an aqueous liquid preparation comprising, in an aqueous solution, an active ingredient consisting of (+)-(S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butyric acid (i.e., bepotastine) or a pharmaceutically acceptable acid addition salt thereof, and a water-soluble metal chloride in a light stabilizing effective amount of 0.2 w/v% or more (see claim 1).

Kita et al teach that the benzenesulfonic acid salt or benzoic acid salt of (S)-4-[4-[(4-chlorophenyl)(2-pyridyl)methoxy]piperidino]butanoic acid (i.e., bepotastine) is excellent in antihistaminic activity and antiallergic activity, has little hygroscopicity and excellent in physicochemical stability, so that it is particularly suitable compound as a medicine. Kita et al also teach that its present invention relates to a medical composition containing the compound as an effective ingredient (see col. 1, lines 10-22).

While Kita et al teach a medical composition comprising bepotastine, Kita et al do not specifically teach how the composition is formulated, and do not specifically teach a water-soluble metal chloride in a light stabilizing effective amount of 0.2 w/v% or more.

Lehmussaari et al teach an ophthalmic composition in the form of a topical aqueous solution consisting essentially of an ophthalmologically active agent containing basic groups, an ion sensitive hydrophilic polymer containing acidic groups, and at least one salt selected from the group of inorganic salts and buffers in a total amount of from

0.01 to 2.0% by weight (abstract). The ophthalmologically active agent may be an antiallergic agent containing basic groups, including basic heterocycles, such as pyridine and piperidine (col. 4, lines 2-9). The salt/buffer functions as a viscosity reducing agent; choices of salts include sodium chloride and potassium chloride (col. 3, lines 45-50 and claim 5). The composition is administered as a liquid and obtains a desired beneficial effect of the active agent in the eye, while simultaneously reducing any discomfort in the patient's eye, as compared to the administration of a composition in gel form. The composition also provides for an additional wetting effect while providing for a better contact and thus a controlled absorption of active agent into the eye (col. 2, lines 10-18).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to formulate the medical composition of Kita et al with the aqueous solution of Lehmussaari et al; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the aqueous solution of Lehmussaari et al provides the benefits of better contact and controlled absorption of active agent into the eye, as well as additional wetting effect, as taught by Lehmussaari et al (col. 2, lines 10-18). One would reasonably expect success from the use of the formulation of Lehmussaari et al to formulate the medical composition of Kita et al because Lehmussaari et al teaches that the opthalmalogically active agent may be an antiallergic agent containing basic groups such as pyridine and piperidine, and Kita et al teach that its compounds have excellent antiallergic activity, and contain both pyridine and a piperidine groups.

Regarding the limitations, "a water-soluble metal chloride in a light-stabilizing effective amount of 0.2 w/v% or more" (claim 1), "sodium chloride at not less than 0.2 w/v% and not more than 0.8 w/v% in a light-stabilizing effective amount" (claim 10), and "light-stabilized with a water-soluble metal chloride at not less than 0.2 w/v% (claim 13), as well as other particular amounts claimed (claims 2, 4, and 13), Lehmussaari teaches an amount of buffer/salt from 0.01 to 2.0% by weight (col. 2, lines 65-67) which functions to reduce the viscosity, which is favorable for both efficacy and ease of application (col. 3, lines 35-40). This range overlaps those of the claimed invention; one skilled in the art would be motivated to manipulate the amount of salt from within said ranges, including the ranges claimed, by routine experimentation, in order to optimize the viscosity reducing effect of the salt. Such amounts would necessarily be a light-stabilizing effective amount, as evidenced by Applicant's specification (e.g., see page 2, line 27 – page 3, line 10).

Regarding the choice of metal chloride (claims 3, 10, and 12) Lehmussaari et al teach six choices of buffer/salt, two of which are sodium chloride and potassium chloride (col. 3, lines 45-50), and exemplify sodium chloride as the salt present in the composition (col. 5, Example 2).

Regarding claims 5 and 6, Kita et al teach the benzenesulfonic acid salt of bepotastine (col. 1, lines 11-13).

Regarding claim 7, Lehmussaari et al teach that the pH of the composition is suitably from 5 to 8 (col. 3, lines 59-60), which is within Applicant's range.

Regarding the limitation that the composition is an eye drop (claims 8, 10 and 13), Lehmussaari et al teach that its invention is an easy-to-use eye drop formulation with improved patient compliance (col. 2, lines 3-5).

Regarding the limitation that the composition is a nasal drop (claim 9), said limitation recites an intended use of the composition. Since the components of the composition of the combined references are suitable for use in the nose, said composition would be capable of use as a nasal drop.

Response to Arguments

6. Applicant's arguments filed 5/19/11 have been fully considered but they are not persuasive.

Applicant argues the combination of Kita and Lehmussaari would not have led to predictable results, adding that a person of ordinary skill in the art would not have been motivated to select a metal chloride from all of the salts and buffers disclosed in Lehmussaari and then manipulate the amount of salt and/or buffer to arrive at 0.2% w/v% from the "broad range" of 0.01-1.5%. Applicant argues that the objective of adding a salt is different between the present application and Lehmussaari (pages 2-3 of Remarks filed 5/19/11).

This argument is not persuasive. Regarding the choice of metal chloride, Lehmussaari specifically names only six viscosity reducing agents, the first two named being metal chlorides (col. 3 , lines 45-50), and therefore one skilled in the art would clearly envisage the use of a metal chloride. Secondly, Applicant's amount of metal

chloride in claim 1 is not 0.2 w/v%, but rather 0.2 w/v% **or more**, which is actually broader than the range disclosed in Lehmussaari. Of the range disclosed in Lehmussaari, Lehmussaari teaches that its disclosed range functions to reduce viscosity, and thus it would be within the purview of the skilled artisan to manipulate the amount of viscosity reducing agent within said range, including amounts of 0.2 w/v% or more, by routine experimentation, in order to optimize the viscosity reducing effect of the viscosity reducing agent. It is noted that the prior art need not optimize amounts for the same reasons as Applicants. Applicants have not argued the criticality of the claimed range, or that amounts within the range of Lehmussaari but outside the claimed range of Applicants would not possess the properties claimed by Applicants.

In response to Applicant's arguments that the results in the specification demonstrate more stability with sodium chloride rather than a buffer, while Lehmussaari teaches a preferred use of a buffering salt to a metal chloride for appearance and storage purposes (page 3 of Remarks), it is noted that, while Lehmussaari does teach a preferred use of a buffer, it does not teach that a metal chloride may not be used, and therefore one skilled in the art would still consider a metal chloride to be useful, albeit perhaps not as preferred. However, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). As noted above, Lehmussaari specifically names only six viscosity reducing agents, the first two named being metal chlorides (col. 3 , lines 45-50), and therefore one skilled in the art would clearly envisage the use of a metal chloride.

Therefore, it is the Examiner's position that the claims are rendered obvious.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Joanne Hama/
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